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ORIGINAL RESEARCH

The relationship between COVID-19 and *Helicobacter pylori* infections in Zawia, Libya, and their effect on certain blood parameters

Fawzia Shawesh[1]*, Ettiyeb Lagha[1], Khadija Alkadea[1], Abdurraouf Zaet[2]

[1]Department of Medical Laboratories, Faculty of Medical Technology, University of Zawia, Libya.
[2]Department of Dental Technology, Faculty of Medical Technology, University of Zawia, Libya.

ABSTRACT

Purpose: Pathogens linked to the most prevalent bacterial and viral infections worldwide are COVID-19 and *Helicobacter pylori (H. pylori)*. The co-infection of COVID-19 and pathogenic microorganisms posed a serious health risk. Several haematological parameters, including platelets, white blood cell total count, lymphocytes, neutrophils, (along with neutrophil-lymphocyte and platelet-lymphocyte ratios), and red blood cells, have also been linked to the presence and severity of COVID-19 infection. This study aims to evaluate the association between COVID-19 Infection and *H. Pylori* infection and their effects on some blood cell counts.

Materials and Methods: One thousand three hundred twenty (1320) COVID-19- infected patients and their blood parameters were examined by ELISA then all data statistics were analyzed.

Results: The percentage of *H. pylori* infection in COVID-19 patients was significantly high in females compared to males (56.30% and 43.70% respectively) (P=0.05) Moreover, there was a significant increase in WBCs (P=0.01), Neutrophil (P=0.004) and platelet counts (P=0.002) count with COVID-19 and *H. pylori* compared to the healthy group. However, there was a significant decrease in counts of lymphocytes (P=0.01), and RBC counts (P=0.03) between all the comparative groups.

Conclusion: There was a significant correlation between *H. pylori* infection and COVID-19 patients. Also, there was a significant difference (x^2 = 2.47, p = 0.03) between all groups according to blood parameters. *(Open J Bio Med Res 2022;1:2-6.)*

Keywords

COVID-19, *Helicobacter pylori*, co-infection, haematological parameters.

AUDIOABSTRACT

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Corresponding Author:

Dr. Fawzia Shawesh

Department of Medical Laboratories, Faculty of Medical Technology, University of Zawia, Libya.

Email: fawziashawesh@zu.edu.ly

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INTRODUCTION

In Wuhan, Hubei province, China, in December 2019, multiple cases of pneumonia with no known cause were reported by Chinese officials.[1] This pneumonia started with severe acute respiratory infection symptoms, and some patients developed acute respiratory distress syndrome, acute respiratory failure, and other catastrophic consequences very quickly.[2,3] The WHO later designated this new CoV as 2019-nCoV after the Chinese Center for Disease Control and Prevention (CDC) discovered it in a patient's throat swab sample in January.[4] The disease spread quickly due to its highly contagious nature, and the WHO immediately declared it to be a public health emergency of global significance. The WHO classified the outbreak as a pandemic as of March 2020.[4]

An essential starting point and promoter of stomach carcinogenesis is *H. pylori* infection because of its contribution to the setting of a chronic state of inflammation, which may evolve toward atrophy of the glands, intestinal metaplasia (IM), and gastric cancer. According to Correa's cascade, noncardiac gastric cancer development goes through a series of mucosal changes from non-atrophic gastritis to atrophic gastritis (AG), IM, dysplasia, and adenocarcinoma. Although the elimination of *H. pylori* may cause AG to regress, the appearance of IM may mark the end of this progression of pathogenic alterations.[5] Therefore, IM

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is a clinically significant lesion that develops following the onset of chronic inflammation brought on by *H. pylori* infection.[6] The high burden of IM in *H. pylori*-infected patients is particularly relevant because of the increased expression of SARS-CoV-2 entry receptors ACE2 and TMPRSS2 in the affected gastric mucosa, mainly due to the migration of intestine-specific cell types, including enterocytes, within the gastric lining.[7]

Additionally, gastric mucosa with IM usually occurs alongside parietal cell loss, leading to an elevation of intragastric juice pH. Consequently, the SARS-CoV-2 virus does not become inactivated by the low pH of the stomach acid[8] some evidence suggests that *H. pylori* infection is related to a diverse and wide range of extra gastric diseases, which are particularly important in the context of COVID-19, including neurological, dermatological, cardiovascular, metabolic, ocular, allergic, renal and respiratory diseases.[9,10] Furthermore, *H. pylori* infection reduced endothelial function by a variety of mechanisms, including an increase in the formation of reactive oxygen species, oxidative stress, decreased nitric oxide formation, expression of cytokines and microRNAs, lipid and glucose metabolism abnormalities, and activation of exosome-mediated pathways.[11,12] Eradication of *H. pylori* also markedly enhanced endothelium-dependent vasodilation in *H. pylori*-infected patients and mice. Therefore, *H. pylori*-infected subjects display a dysfunctional basal endothelial state that could be substantially aggravated when the subject is infected with SARS-CoV-2.

It is now reported that the angiotensin-converting enzyme-2 (ACE-2) receptors are a binding site for the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2).[13] These receptors are highly expressed in the intestine, suggesting that SARS-CoV-2 infection may lead to gastrointestinal symptoms among patients with COVID-19. As *H. pylori* increase ACE-2 receptor expression in the gastrointestinal tract, a study conducted in turkey investigating the effects of *H. pylori* on the clinical presentation and course of COVID-19 infections showed that patients with *H. pylori* infection had significantly more frequent abdominal pain (P =.007) and diarrhea (P =.006) than negative *H. pylori* patients. While severity COVID-19, outcomes of the disease, and the number of hospitalized days were not significantly associated with *H. pylori* infection.[14] Another supportive study that investigated stomach susceptibility factors for SARS-CoV-2 showed that IM and *H. pylori* infection history may be susceptibility factors of SARS-CoV-2, and the mucosal protective agent may be useful for the blockade of SARS-CoV-2 transmission from the stomach to the intestine.[15] Moreover, another study showed that COVID-19 infection was more frequent in males than females, especially between 15-25 years, and also showed COVID-19 patients with positive results to *H. pylori* have higher levels of neutrophils (p-value= 0.001) and lymphocytes (p-value 0.032) respectively.[16] In general, in Arabic countries, few studies have been conducted to determine whether there is a connection between Covid-19 and *H. pylori*. Also, particularly, in Libya, neither has been done. Therefore, the objective of the current study was to determine the correlation between *H. pylori* in COVID-19 patients.

MATERIALS AND METHODS

The present experimental study involved 1320 COVID-19- infected patients from several COVID-19 Centers in Zawia, Libya from Mars to August 2021. A control group of (130) seemingly healthy people of similar ages and sexes. COVID-19-infected patients were confirmed by Reverse Transcription Polymerase Chain Reaction (PCR) device. Research procedures were supervised by the communication medical doctor of the COVID-19 isolation centers in Zawia city. The sterilized 5mL blood samples were acquired from the participants, formerly divided into two types of tubes: plane tubes and EDTA tubes. Each collected blood in an EDTA tube was used for a complete blood count test (CBC), and the plane tube samples were subjected to evaluate *H. pylori* infection (anti-HP IgG) antibody detection. All study groups were examined for Anti-HP IgG using ELISA kits. The ELISA results were calculated as indicated in the manufacturer's instructions. To evaluate white blood cell (WBC) counts, particularly neutrophils, lymphocytes, and platelet. The samples were processed by the equipment, and total WBCs and neutrophils are automatically computed.

All data statistics were collected and analyzed using the application of the statistical package of social science (SPSS) V. 25. Comparison of the mean value of continuous data was tested by ANOVA test. t-test and Chi-square statistical analyses were performed to detect significant values. The P-value of ≤ 0.05 was statistical significance.

RESULTS

All the Patients' age ranged from 17 to 82 years. The distribution of COVID-19 patients according to gender involved in this study was shown in Fig 1. Females were higher infected with COVID-19 compared to males. Moreover, the percentage of *H. pylori* infection in COVID-19 patients was significantly high in females compared to males (56.30% and 43.70% respectively) (P=0.05) as shown in Fig 2.

Table 1 presents that there was a significant correlation between *H. pylori* infection and COVID-19 patients. There was a high correlation between anti-*H. pylori* IgG and in COVID-19 patients in all age groups. Overall, the statistical analysis revealed a high presence of COVID-19 and *H. pylori* was (56.1%) P=0.01. The highest percentage of association was 29.76% in patients aged 17-27 years, followed by (24.05%) in the 39-49 age group. Whereas, the oldest age of patients (72-82 years) has the lowest coinfection of *H. pylori* and COVID-19 (7.02%).

As Table 2 shows, there was a significant difference (x^2 = 2.47, P= 0.03) between all groups according to blood parameters. Firstly, there was a significant increase in WBCs count with COVID-19 and *H. pylori* compared to the healthy group (P=0.01). Second, there was a similar increase in Neutrophil counts (P=0.004), and platelet counts (P=0.002). However, there was a significant decrease in counts of lymphocytes (P=0.01), and RBC counts (P=0.03) between all the comparative groups.

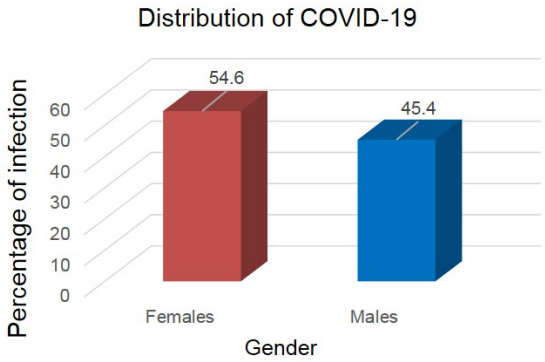

Fig 1. Distribution of COVID-19 in this study according to gender.

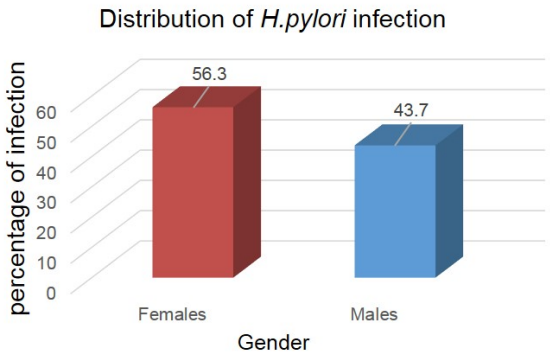

Fig 2. Distribution of *H. pylori* and COVID-19 in this study according to gender.

Table 1. Frequency of *H. pylori* infection and COVID-19 patients according to the age groups.

Age group (years)	COVID-19 N (%)	*H. pylori* N (%)	Statistical analysis
17-27	387 (29.32%)	220 (29.76%)	
28-38	230 (17.42%)	108 (14.59%)	t. test = 2.13,
39-49	320 (24.24%)	178 (24.05%)	df =1.9,
50-60	123 (9.32%)	122 (16.48%)	P = 0.01
61-71	140 (10.6%)	60 (8.1%)	
72-82	120 (9.1%)	52 (7.02%)	56.1%
Total	1320	740	

df=Degree of freedom

Table 2. Comparison of some blood parameters in COVID-19 and *H. pylori* patients and control group.

Parameters	COVID-19 patients (Cells count) (Mean ±SD)	*H. pylori patients* (Cells count) (Mean ± SD)	Control group (Cells count) (Mean ± SD).	P-value
WBCs ($X10^3/\mu L$)	12.63 ± 0.25	8.75 ± 0.45	6.252 ± 0.198	0.01*
Neutrophil ($X10^3/\mu L$)	91.33±13.50	60.12±10.23	49.81±4.45	0.004**
Lymphocyte ($X10^3/\mu L$)	15.50±5.21	13.30± 4.28	21.32±3.97	0.01*
Platelets ($X10^3/\mu L$)	560.2 ± 50.56	265.62± 7.28	297.94± 7.22	0.002**
RBCs ($X10^6$/mm3)	3.01 ± 0.053	3.67±0.043	4.964± 0.061	0.03*

SD = Standard deviation

DISCUSSION

To the best of our knowledge, this is the first data analysis in western region in Libya which are investigating the association between COVID-19 infection and *H. Pylori* infection and their effects on some blood cell counts. Our meta-analysis consisted of 1320 COVID-19- infected patients and confirmed by PCR test. Numerous studies conducted between 1965 and 2021 attempted to determine the correlation between *H. pylori* infection and respiratory illnesses like bronchiectasis, TB, cystic fibrosis, lung cancer, sarcoidosis, bronchial asthma, and COPD.[17] Moreover, 10 eligible studies with 54,218 cases revealed that those with blood group O had a considerably reduced propensity to get COVID-19 than those with blood groups A and B, which are thought to enhance the likelihood of infection.[18]

The hematopoietic system plays a prominent role in the 2019 coronavirus disease. Patients who have COVID-19 have been reported to have widespread hematopoietic abnormalities. Haemoglobin, eosinophils, and basophils have all significantly decreased since the disease's early stages, and this has been linked to the severity of the condition and its clinical outcome. As SARS-CoV-2 infection of monocytes appears to directly impact the anti-viral adaptive immune responses, the kinetics of monocytes in COVID-19 infection are now still unknown.[19]

Patients with COVID-19 have lower hemoglobin levels and pathologically higher ferritin concentrations.[19] Huang et al found reduced haemoglobin concentrations in 38% of the study population admitted to the hospital.[20] While, Wang et al. found that the haemoglobin values reduced (<110 g/L) in 19% of the hospitalized patients.[21] In this instance, the variation in age structure between the populations from the two studies may be used to explain the increased incidence of a low hemoglobin concentration in COVID-19 patients as indicated by Huang. In actuality, the study population described by Wang et al had a median age of 42 (33-53) but Huang et al provided results from a population aged 56 (26-88). As we mentioned above there was a significant correlation between anti-*H. pylori* IgG in COVID-19 patients in all age groups. In this analysis, (29.76%) of the infected patients, their median age of 17-27 years while (24.05%) were in 39-49 years. However, (7.02% of) those infected by COVID-19 and *H. pylori* were between 72- 82.

The present study showed that females were higher infected with COVID-19 compared to males furthermore, females who have been infected with COVID-19 also have a higher percentage of *H. pylori*-infected (56.30%) than infected males (43.70%) with (P=0.05). However, the findings of the current study do not support the previous study, which found that males were more likely than females to be infected with COVID-19, particularly between the age group (15-25).[16] A possible explanation for these results may be that the viral load, the severity of the sickness, and death could all be affected by this modification in immunity. Additionally, these gender differences might be influenced by hormone milieus and serve as a predictor of viral infections.

Moreover, according to the blood parameters, this study found were significant increase in WBCs count in patients who were co-infected with COVID-19 and *H. pylori* compared to healthy groups P=0.01. Whereas there was a similar increase in the neutrophil and platelet count P=0,004 and P=0.002 respectively. However, the analysis showed a decrease in lymphocytes P=0.01 and RBC counts P=0.03 among all the comparison groupings. The present findings seem to be consistent with other research which have shown similar results.[16,22,23] These factors may explain the relatively good correlation between WBC counts, lymphocytes, and neutrophils which are frequently observed in COVID-19 patients. Also, these blood conditions were associated with the severity of the illness. This distinguishes this condition from ordinary viral infections, where neutrophils are abnormal numbers and lymphocytes are often higher.[22,23] It may also be important for survival to have the capacity to restore lymphocytes, especially T-lymphocyte cells, which are damaged by the virus.[16,20]

CONCLUSION

The connection between COVID-19 and *H. pylori* IgG antibodies suggests that COVID-19 infection may be more contagious in *H. pylori*-infected patients than in the general population.

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